PCT/EP2003/007068

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 30530003WO	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/EP2003/007068	International filing date (*day/month/year*) 02 July 2003 (02.07.2003)	Priority date (*day/month/year*) 02 July 2002 (02.07.2002)
International Patent Classification (IPC) or national classification and IPC C12N 1/06, C12P 21/00, C12N 15/12, C07K 14/47		
Applicant NOVOLOGIX GMBH		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

   ☒ Box No. I Basis of the report
   ☐ Box No. II Priority
   ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   ☐ Box No. IV Lack of unity of invention
   ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   ☒ Box No. VI Certain documents cited
   ☒ Box No. VII Certain defects in the international application
   ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand 29 January 2004 (29.01.2004)	Date of completion of this report 09 July 2004 (09.07.2004)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2003/007068

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☒ the description:

pages 1-12, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

pages 1-22, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the drawings:

pages 1/15-15/15, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2003/007068

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-6, 8-22, 7 (partly)

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 1-6, 8-22, 7 (partly) are so unclear that no meaningful opinion could be formed *(specify)*:

See the supplemental box

☒ the claims, or said claims Nos. 1-6, 8-22, 7 (partly) are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 1-6, 8-22, 7 (partly).

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ see Supplemental Box for further details.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of:

This report makes reference to the following documents:

D1: DE 199 29 485 A (FRAUNHOFER GES FORSCHUNG) 11 January 2001 (2001-01-11)

D2: SONG H ET AL: 'Crystal structure of intact elongation factor EF-Tu from Escherichia coli in GDP conformation at 2.05 A resolution' JOURNAL OF MOLECULAR BIOLOGY 22 JAN 1999 UNITED KINGDOM, Vol. 285, No. 3, 22 January 1999 (1999-01-22), pages 1245-1256, XP002270308 ISSN: 0022-2836, mentioned in the application

D3: HEFFRON S E ET AL: "Structure of an EF-Tu complex with a thiazolyl peptide antibiotic determined at 2.35 A resolution: atomic basis for GE2270A inhibition of EF-Tu." BIOCHEMISTRY. UNITED STATES 11 JAN 2000, Vol. 39, No. 1, 11 January 2000 (2000-01-11), pages 37-45, XP001172470 ISSN: 0006-2960

D4: HOGG T ET AL: "Inhibitory mechanisms of antibiotics targeting elongation factor Tu." CURRENT PROTEIN & PEPTIDE SCIENCE. NETHERLANDS FEB 2002, Vol. 3, No. 1, February 2002 (2002-02), pages 121-131, XP002270310 ISSN: 1389-2037.

The present application relates to a use of substances that bind to components of the cytoskeleton for bacterial cell disruption, characterized in that the substances contain the domains 3 of EF-Tu and no other domains of EF-Tu.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III

Since the International Searching Authority did not conduct a search for the valid complete claims 1-6, 8-22 or claim 7, in part, the International Examining Authority likewise has not established a written opinion with respect to the *novelty, inventive step and industrial applicability* of these claims.

The written opinion established with respect to the novelty, inventive step and industrial applicability of claim 7 is restricted to bacterial cell disruption.

INTERNATIONAL PR[redacted]MINARY EXAMINATION REPORT

International application No.
PC[redacted]P 03/07068

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	7, in part	YES
	Claims		NO
Inventive step (IS)	Claims	7, in part	YES
	Claims		NO
Industrial applicability (IA)	Claims	7, in part	YES
	Claims		NO

2. Citations and explanations

1. Novelty

The subject matter of claim 7, which relates to the use of substances that bind to components of the cytoskeleton for bacterial cell disruption, said use being characterized in that the substances contain the domains 3 of EF-Tu and no other domains of EF-Tu, is novel over the prior art.

2. Inventive step

D1, which is regarded as the closest prior art, discloses a method for disrupting bacterial cells using a protein showing lytic enzyme activity, involving an amino acid sequence represented in SEQ ID No. 1, the protein having a molecular weight of 15,000 to 20,000 Da, and at least two proteins, each showing lytic enzyme activity, a protein and at least one further protein being selected from the group consisting of the beta-lytic metallo-endopeptidase of *Lysobacter enzymogenes* and an alpha-lytic protease of *Lysobacter enzymogenes* with an amino acid sequence represented in SEQ ID No. 3,
from which the subject matter of claim 7 differs by the use of substances that bind to components of the cytoskeleton for bacterial cell disruption, said use being characterized in that the substances contain the domains 3

of EF-Tu and no other domains of EF-Tu.

Therefore, the problem to be solved by the present invention can be regarded as that of using further substances for bacterial cell disruption.

Although a person skilled in the art would be prompted by D1 to solve the problem of interest, in view of the prior art, he would NOT consider it obvious to use substances that bind to components of the cytoskeleton for bacterial cell disruption, the use characterized in that the substances contain the domains 3 of EF-Tu and no other domains of EF-Tu.

Therefore, the subject matter of claim 7 is inventive and technically supported, insofar as it is restricted to bacterial cell disruption.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: VI

Certain documents cited

Certain published documents

Application No. Patent No.	Publication Date (day/month/year)	Filing Date (day/month/year)	Priority Date (valid claim) (day/month/year)
WO02087554	07-11-2002	22-04-2002	30-04-2001

As mentioned in the applicant's letter of 28 May 2004, the application PCT/EP02/04410 contains subject matter comparable to that in the present application. PCT/EP02/04410 was published as WO0287554 on 11 July 2002.

WO0287554 discloses the use of substances that bind to EF-Tu to inhibit the formation of a cytoskeleton in bacterial cells, and characterized in that the substances contain sections of the amino acid sequences from the domain 2 and/or 3 with a length of 4 to 20 amino acids.

Said document discloses that if the polymerization of the EF-Tu protein is inhibited at the binding areas denoted in figure 3 by + and - through the addition of a surplus of particles containing sections of the amino acid sequence of domains 2 or 3, it is impossible for the bacterial cells in question to survive, because their cell structure breaks down.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The valid complete claims 1-6, 8-22 and claim 7, in part, relate to the use, method and construct characterized by a desirable unique feature or characteristic, namely the use of substances that bind to components of the cycloskeleton for cell disruption, and methods for cell disruption and construct, involving a sequence that codes for components of the cytoskeleton of cell-destabilizing compounds. Therefore, the claims contain all of the uses that have this unique feature or characteristic, whereas the description in the application provides support within the meaning of PCT Article 5 *only for such a use in E. coli*. In the present case, the claims lack the corresponding support and the application lacks the requisite disclosure to such an extent that a person skilled in the art cannot determine what technical features are essential for carrying out said cell disruption over the entire scope for which protection is sought. D3 and D4 disclose the peptide antibiotic mechanisms of binding and inhibition of the elongation factor EF-Tu (see the abstracts). These peptide antibiotics inhibit protein biosynthesis, thereby leading to the death and immediate cell disruption of the microorganisms. The reworkability of the valid complete claims 1-6, 8-22, and claim 7, in part, have constituted an unreasonable difficulty within the meaning of PCT Article 5 for a person skilled in the art. A person skilled in the art has had considerable difficulty determining what substances, under what conditions, and in what organisms, bind to the EF-Tu in order to achieve the desired cell disruption. He has also had considerable difficulty determining whether the desired cell disruption

VIII. Certain observations on the international application

takes place by inhibition of the protein biosynthesis or by cytoskeleton synthesis, as claimed.

The above notwithstanding, the claims also lacks the requisite clarity, as stipulated in PCT Article 6, with respect to the technical features necessary for their use in the desired cell disruption over the entire scope of protection sought for the valid complete claims 1-6 8-22, and claim 7, in part.

These observations confirm the reasons for which the International Searching Authority did not conduct a search for the valid complete claims 1-6, 8-22 and claim 7, in part.